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(54) Title: REDUCTION OF LATEX ASSOCIATED HYPERSENSITIVITY

(57) Abstract

Hypersensitivity to latex containing products is reduced or eliminated by coating or combining such products with an anti–hypersensitivity agent which includes chitosan, chitosan derivatives, anti–inflammatory agents or combinations thereof.

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REDUCTION OF LATEX ASSOCIATED HYPERSENSITIVITY

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application Serial No. 60/121,486 filed February 24, 1999.

1. Field of the Invention

The present invention relates to methods and materials for reducing or eliminating hypersensitivity reactions such as dermatitis and allergic reactions associated with latex.

2. Description of Related Art

Latex containing products are widely used in industry and by consumers. Latex was originally isolated from plants, e.g., *Havea braziliensis*. Natural latex is typically made of globules of rubber hydrocarbon coated with protein and usually contains about 60% water, 35% hydrocarbon, 2% protein and relatively low percentages of sugars and inorganic salts. Compounding ingredients such as stabilizers and thickeners may be utilized in compounding latices. In addition, latex can be coagulated by treatment with electrolytes, freezing temperatures, or acid and concentrated by evaporation or centrifugation. Latex may be formed or processed into useful thin films or other configurations. A vulcanized form of natural latex is available in which vulcanizing ingredients cause the solid phase deposited from latex to become cross-linked when suitable conditions such as elevated temperature are established. Synthetic latexes are made by emulsion polymerization techniques from polychloroprenes, polystyrenes, polybutadienes, styrene-butadiene copolymers, acrylate resins, and polyvinyl acetate. Additives include protective colloids, stabilizers, thickeners, pigments and vulcanization aids.

Latex is endowed with beneficial chemical and physical characteristics which promote widespread use of latex products. Such characteristics are well known and include, e.g., resistance to permeability of liquids such as water, alcohol, bodily secretions, etc., resistance to corrosion, and elasticity, i.e., the ability to return to

original size and shape after compressing or stretching. As a result, articles made from latex products have found use in a number of industries, e.g., medicine as, e.g., gloves, catheters, bandages and condoms.

Unfortunately, an increasing number of individuals are exhibiting hypersensitivity to latex. It is believed that, in the case of natural latex, naturally occurring proteins and other antigenic constituents cause allergic reactions ranging from rash to life-threatening analphylactic shock. Due to the wide spread use of latex in medicine, the number and severity of allergies among hospital personnel is constantly increasing. Often, allergies of the immediate type to natural latex are involved. In addition, vulcanizing aids which may be present in latex gloves, for example thiurams, can cause contact allergies.

Surgical gloves can be manufactured by providing hand-shaped molds or mandrels onto which a film forming latex is deposited by dipping or the like. A mold-releasing powder is usually dusted first onto the mold to facilitate removal of the molded material from the mold. It is a usual practice to apply a lubricating substance onto the outside of the molded glove, so that when the finished glove is peeled from the mold and retroverted, the interior of the glove is thus coated with a layer of lubricating powder for ease in donning the glove. Particles of the mold-releasing powder frequently remain on or entrapped in the exterior surface of the surgical glove and may be the cause of hypersensitivity. Sensitization may be caused by skin contact or by inhalation of glove powders, which may generally contain allergens. When gloves are used, some glove powder including latex and other substances can become airborne and then inhaled. In this way the skin barrier is bypassed and the risk of occurrence of allergies is distinctly increased. Furthermore, the moist, warm conditions in the glove offer ideal growth conditions for microbes, leading to microbial growth inside the glove in the case of prolonged operation times. The "glove broth" that accumulates in the case of perspiration can migrate from gloves that are not intact or perforated and can result in a threat to the patient.

As a result, techniques to reduce or eliminate hypersensitivity reactions to latex have been developed. For example, U.S. Pat. No. 5,741,885 is directed to methods for reducing allergenicity of natural rubber latex articles and U.S. Pat. No.

4,540,407 is directed to surgical gloves and surface treatment of surgical gloves for avoiding starch peritonitis and the like. Due to the increasing incidence of hypersensitivity reactions to latex products, the need for additional techniques to reduce or eliminate such reactions is continuing.

SUMMARY OF THE INVENTION

An article of manufacture is provided which includes latex and an effective latex hypersensitivity reducing amount of an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof.

Also provided is a protective sheath having a layer of material manufactured from latex and a coating of an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof.

A method of reducing latex hypersensitivity reaction in an individual is provided which includes providing an article containing latex; coating the article with an effective amount of an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof; and exposing the individual to the coated article.

Also provided is a method of manufacturing a latex article having reduced hypersensitivity associated therewith which includes contacting and adhering the latex article with an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof.

A method of binding water in a latex protective sheath which contacts skin is provided which includes contacting and adhering chitosan or a chitosan derivative to a surface of the sheath which is intended to contact skin in an amount effective to absorb water.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The property of latex containing articles to promote hypersensitivity reactions including allergy, dermatitis or any other idiosyncratic reaction of an individual to latex or materials used to process latices or latex articles is reduced according to the present invention by treating such articles with an effective amount of an anti-hypersensitivity agent as defined herein. In one aspect, the anti-hypersensitivity agent forms a protective film between the latex and skin or other latex contacting tissue. In another aspect, the therapeutic action of the anti-hypersensitivity agent acts to block or reduce a sensitive individual's response to latex or materials used to process latices or latex articles. In yet another aspect, the anti-hypersensitivity agent combines a protective film forming property with therapeutic action to block or reduce a sensitive individual's adverse response.

Accordingly, in one aspect, chitosan and/or chitosan derivatives are utilized as active ingredients for anti-hypersensitivity finishing of latices, specifically for coating of latices. Through the surface treatment of latices, especially of protective sheaths such as latex gloves for the industrial or surgical sector, bandages and condoms, a protective film is created between skin or other body tissue and the potential allergens or other irritants in the latex, which if it does not completely exclude the possibility of precipitating a hypersensitivity reaction, nevertheless significantly reduces it. It should be understood that a film formed from chitosan or a chitosan derivitation may adhere to skin, latex, both or neither. Moreover, a thin chitosan film can function as a "care polymer", i.e., it provides a pleasant skin feel and improved sliding ability. As a result of the bacteriostatic and bacteriocidal properties of the chitosans, the effect of glove disinfection is prolonged, since bacterial growth is stopped or at least retarded during the time the gloves are worn. Through these measures, the risk of hypersensitivity for the user and the risk of infection for the patient are distinctly reduced. It is contemplated that coating of the latices can take place in any conventional manner known to those skilled in the art; preferably the semifinished products or end products are dipped into an aqueous solution of the chitosans or sprayed with this and then dried.

Thus, latex containing articles are manufactured according to procedures well-known to those skilled in the art. For example, a common manufacturing process well-suited for utilization herein is the dip-forming process. In this procedure, an article forming mandrel typically coated with a coagulating pre-treatment such as water, alcohol, or acetone suspension, is coated with a latex emulsion by dipping the mandrel into a latex emulsion bath or tank followed by rinsing and drying/curing steps prior to removal of the latex article from the mandrel. In some circumstances, the dip-formed latex articles are retroverted or turned inside out to peel or remove them from the forming mandrels. The production of rubber gloves and condoms commonly utilizes such a retroversion step for removal so that the inner surface of the finished article is actually the opposed outer surface of the originally dip-formed product.

In accordance with the present invention, prior to dipping or otherwise applying latex to the mandrel, the mandrel is coated with chitosan or a chitosan derivative which can be in the form of a powder, gel, emulsion, suspension or solution which evaporates to leave a chitosan or chitosan derivative residue. It is contemplated that any method known to those skilled in the art may be utilized to apply chitosan or a derivative thereof to the mandrel. The coated mandrel then receives a coating of latex by dipping, spraying or by any other known suitable coating process. For example, dipping the coated mandrel into a latex emulsion results in a film which congeals to form a glove or other shaped object which is subsequently retroverted. In this manner, the chitosan adheres to the surface of the film adjacent the mandrel and, upon retroversion, the chitosan adhered surface is the exterior surface of the article, i.e., the surface which is exposed to the environment. If the article is removed without retroversion, the chitosan adhered surface is the interior surface of the article, i.e., the surface which contacts, e.g., a hand inserted into the glove.

It is also contemplated that prior to retroversion, chitosan or a derivative thereof may be applied to the outer surface of the latex film, i.e., the surface not in contact with the mandrel, by spraying, dipping, painting or any other known coating method. In this manner, if the mandrel contacting surface has been coated with chitosan or a derivative thereof, both the interior and exterior surfaces of the

article will include chitosan or a derivative thereof. Alternatively, if chitosan or a derivative thereof is not coated on the mandrel surface, only the opposing surface will be made to include chitosan or a derivative thereof.

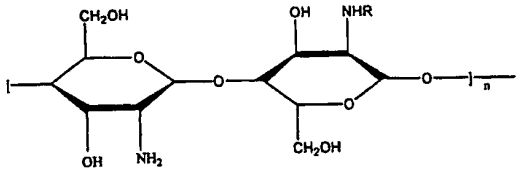
If the latex article is made by injection molding, it is contemplated that chitosan or a derivative thereof can be applied in the form of a powder, gel, emulsion, suspension or solution which evaporates to deposit a chitosan or derivative thereof residue on the mold interior prior to mold injection. Alternatively, the chitosan or derivative thereof may be applied after removal of the article from the mold by coating the surface of the molded article. Indeed, any suitable manner of applying chitosan or a derivative thereof to a latex article is contemplated which does not substantially compromise the integrity of the finished latex product.

In another aspect of the invention, chitosan or a derivative thereof is introduced directly into the latex, for example by joint use of the substance as a vulcanizing aid in the manufacturing of the latices. In this way the number of adverse reactions induced by vulcanizing aids and thus the sensitization potential of latex gloves can be reduced. "Latex" is defined herein to include natural latex and synthetic latex polymers which, for example after coagulation by freezing or by treatment with electrolytes, are precipitated from aqueous dispersions and processed into thin films. The latices, which for example may involve, e.g., rubber, polychloroprenes, polystyrenes, polybutadienes, or copolymers of styrene and butadiene, acrylate resins and polyvinyl acetate may be produced by emulsion polymerization and can contain as additives protective colloids, stabilizers, thickeners, pigments and vulcanization aids. If the chitosans are used as vulcanization aids, they can be used as additives in quantities of about 0.1 to about 2, preferably about 1 to about 1.5 wt% - based on the monomer - introduced into the emulsion polymerization or subsequently introduced into the aqueous or organic latices before these are freed from liquid phase, for example rolled into films, and then processed into the salable products.

In another aspect of the invention, powdered chitosan or derivatives thereof are utilized as water-binding agents in latex gloves. The chitosan or derivatives thereof are capable of absorbing glove broth which may include, e.g., perspiration, microbes and powdered materials used to process the latex into the

finished article, in this way improving the wearing comfort and reducing the risk of skin irritations. In addition, since the free moisture is reduced, bacterial growth conditions are made less favorable, thus leading to a lower infection risk. Such powder preparation forms can serve directly as glove powder or also in a mixture with talc and similar additives.

Chitosans are biopolymers and are included in the group of hydrocolloids. Chemically they involve partially deacetylated chitins of various molecular weights that contain the following - idealized - monomer building block:



In contrast to most hydrocolloids, which are negatively charged in the range of biological pH values, chitosans represent cationic biopolymers under these conditions. The positively charged chitosans can interact with oppositely charged surfaces and are therefore used in cosmetic hair and body care agents as well as pharmaceutical preparations (see *Ullmans's Encyclopedia of Industrial Chemistry*, 5th Ed., Vol. A6, Weinheim, Verlag Chemie, 1996, p. 231-332). Reviews on this topic have also been published by B. Gesslein et al. in *HAPPI27:57* (1990), O. Skaugrud in *Drug Cosm. Ind.* 148:24 (1991) and E. Onsoyen et al. in *Seifen-Olefette-Wachse* 117:633 (1991). For producing chitosans and derivatives thereof, one begins from chitin, for example crustacean shell residues, which are available in large quantities as inexpensive raw materials. The chitin is deproteinated in a well-known process first described by Hackmann et al., usually first through the use of bases, demineralized by addition of mineral acids, and finally deacetylated by addition of strong bases, wherein the molecular weights can be distributed over a broad spectrum.

Corresponding processes are known for example from *Makromol. Chem.* 177:3589 (1976) or the French Patent Application FR-A-2701266. It is contemplated that the average molecular weight of chitosan or chitosan derivatives may range from about 25,000 daltons to about 5,000,000 daltons. Preferably such

types are used as are disclosed in German Patent Applications DE-A1 4,442,987 and DE-Al 19, 537,001 (Henkel) and which have an average molecular weight of about 25,000 to about 500,000 or about 800,000 to about 1,200,000 dalton, a viscosity according to Brookfield (1 wt% in glycolic acid) of less than about 5,000 mPas, a deactylation degree in the range of about 80 to about 88%, and an ash content of less than about 0.3 wt%. In addition to chitosan as a typical cationic biopolymer, or its salts, in the sense of the invention anionic and nonionic derivatized chitosans are known, for example carboxylation, succinylation, or alkoxylation products come under consideration, as described for example in German Patent DE-C2 3,713,009 (L'Oreal) as well as German Patent Application DE-A1 19,604,180 (Henkel).

In another aspect of the present invention, latex hypersensitivity is reduced or eliminated by coating a latex article with an anti-inflammatory agent. Any coating method known to those skilled in the art is contemplated including, e.g., the coating processes described above. Anti-inflammatory agent, as used herein, includes substances which may have more than anti-inflammatory activity such as anti-allergy therapeutics, e.g, antihistamines and steroids.

Thus, it is contemplated that any compound having anti-inflammatory activity may be utilized in accordance with the present invention. Examples of substances having anti-inflammatory activity include but are not limited to steroidal and nonsteroidal anti-inflammatories such as indomethacin, ibuprofen, alpha hydroxy acids, vitamin A derivatives, vitamin E derivatives, orange peel wax, ascorbylpalmitate, lipon acid -dihydrolipon acid, bifidus-baktera, D-panthenol, jojoba, cyclo-adenosinmonophosphate, alpha tocopherol, ascorbic acid, 2,4-hexadien-1-ol, hydrocortisone, naproxen, glycosaminoglycans, dl-alpha-tocopherol nicotinate, linola-fat, aloe vera, azelaic acid, acetylsalicylic acid, phenylbutazone, alpha-bisabolol, 6(3-(1-adamantyl)-4-methoxyphenyl) 2-naphtoic acid, meristem extract, triacontanol, diprolene, lipoplastidine, unipertan, isotretinoin, enterobacter-hafnia extract, BW 540C, shikonin, extract from hypericum perforatum, ferula acid, coffee acid-3-methylester, 4-hydroxy-3-methoxyzimt acid, hibisci flos, 18-b glycyrrhetin acid (gl-a), lipids, strontium salts, li-salts, ca-salts, azeptin, CAS No. 58581-89-8, cyclosporin, serotonin, sulfosuccinic acid ester, 2(1h)- oxo-1-phenyl-1,8-

naphthyridine-3-carboxamides, pyridooxazinedione phenyl intermediate, hydroxy oxo phenyl naphthridine carboxamide, 2-aminothiazole 106-50-3, 1,4-diaminobenzene, 3-aminopyridine 504-24-5, 4-aminopryridine 1990-90-5, 4-amino-3-methylpridine 3731-52-0, 3-pyridinemethanamine 3731-53-1, 4-pyridylmethylamine 4319-49-7, 4-aminomorpholine 5049-61-6, pyrazinamine 5350-93-6, 5-amino-2-chloropyridine 6628-77-9, 5-amino-2-methoxypyridine 50541-93-0, 4-amino-1-benzylpiperidine, 4-nitrophenyl isocyanate 103-71-9, phenyl isocyanate, reactions 104-12-1, 4-chlorophenyl isocyanate 622-58-2, 4-tolyl,isocyanate 700-87-8 5416-93-3, 4-anisyl isocyanate 18908-07-1, 3-anisyl isocyanate (addn. reaction of, with, hydroxyphenylnapthyridinone), 504-29-0, 2-aminopyridine, (carbamoylation of, with Et malonyl chloride), 36239-09-5, ethyl, malonyl chloride (carbamoylation of, with aminopyridine), 503-38-8,, trichloromethyl chloroformate (cyclocondensation of, with anilinoniotinate), 105-53-3, diethyl malonate (cyclocondensation, of, with phenylpyridooxazinedione),51269-84-2, methyl,2-anilinonicotinate (cyclocondensation of, with trichloromethyl, chloroformate), 89109-17-1p (prepn. and addn. reaction of, with isocyanates), 138305-19-8p (prepn. and cyclocondensation of, with, di-et malonate and) ethoxycarbonyl)pyridylacetamide, 138305-21-2r, (prepn. and cyclocondensation of, with phenylpyridooxazinedione), 302-79-4, trans-retinoic acid 4759-48-2,, 13-cis-retinoic acid, 3899-20-5,, ethyl retinate 55079-83-9, etretin 69427-46-9 13-cis-etretin (arachidonic acid metabolites release by macrophages response to), 506-32-1, arachidonic acid (meta. of, by macrophaged, retinoids, effect on), 13367-85-6, prostaglandin b2 71160-24-2, leukotriene b4, phenylthioethysyndones, achillea millefolium, baicalein, flavone 66000-40-6, pyrrologuinoline, quinone derivs, auriculariaceae, ephedrines, 1-cinnamoyl-2-methyl-5-methoxy-3-indolylacetic acid, antioxidants from zingiber cassumunar, ginger (z. xassumunar, isolation and structure dent. of cassumunarins a and b and c), buddleja extract, Saponins, gersten-treber-extract, premier oil bird, cassumunarin a 155518-36-8p, Cassumunarin b rl, cassumunarin c 155551-80-7p, phytosterol. CAS registry numbers given above identify substances having anti-inflammatory activity which may be utilized herein. Preferred anti-inflammatory compounds herein include corticosteriods, strontium salts and phytosterols.

In operation, the anti-inflammatory agent acts prophylactically and/or actively to prevent, reverse or reduce symptoms from an adverse reaction based on hypersensitivity to latex or materials used in processing latex. The anti-inflammatory agent is absorbed topically and can be applied to the latex article in association with known pharmaceutically acceptable vehicles which facilitate transdermal delivery.

In another aspect of the present invention, chitosan or a derivative thereof and an anti-inflammatory agent as defined above are coated in combination as an anti-hypersensitivity agent on a latex article. The manufacturing procedures of latex containing articles described above are suitable for use in connection with this aspect of the present invention. Likewise, the points at which the anti-hypersensitivity agent can be applied to the latex article during the manufacturing process correspond.

A benefit of combining chitosan or a derivative thereof with an anti-inflammatory agent is that chitosan is known to increase effectiveness of transdermal delivery of therapeutic agents. Accordingly, the combination may be applied as a powder, a gel or as a mixture which is suspended, emulsified or in solution. When a powder vehicle is desired, an effective amount of a powdered anti-inflammatory agent is mixed with chitosan powder using pharmaceutically acceptable techniques such as trituration, milling and the like until a uniform mixture is obtained. Liquid anti-inflammatory agents may be adsorbed onto powders such as talc prior to mixing. Pharmaceutically acceptable diluents and excipients may be incorporated if desired. The powder may be applied to the mandrel, latex article, or both as described above. In a preferred embodiment, an anti-inflammatory agent is mixed with a chitosan gel having about 1% to about 2% by weight of chitosan which is applied as a coating to either a mandrel, an external surface of a congealing latex article or to both. Preferred anti-inflammatory agents for combination with chitosan or derivatives thereof include corticosteroids, strontium salts and phytosterols.

It will be understood that various modifications may be made to the embodiments and aspects disclosed herein. For example, it is contemplated that various adjuvants such as emollients, moisturizers and other compatible skin care formulations may be combined with the above-descried anti-hypersensitivity agents as a coating for latex articles. In addition, it is contemplated that any combination of the

above described chitosans and anti-inflammatory agents may be combined, e.g., two or more anti-inflammatory agents may be combined for complementary or synergistic effects and/or chitosan may be mixed with chitosan derivatives in various formulations. Therefore, the above description should not be viewed as limiting, but merely as exemplifications of preferred embodiments. Those skilled in the art will envision other modifications within the spirit and scope of the claims appended hereto.

WHAT IS CLAIMED IS:

1. An article of manufacture comprising latex and an effective latex hypersensitivity reducing amount of an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof.

2. An article of manufacture according to claim 1 wherein the article of manufacture is selected from the group consisting of glove, bandage and condom.

3. An article of manufacturer according to claim 1 wherein the anti-inflammatory agent is selected from the group consisting of corticosteriods, strontium salts and phytosterols.

4. An article of manufacture according to claim 1 wherein the chitosan or chitosan derivative have an average molecular weight of about 25,000 to about 500,000 daltons, a Brookfield viscosity (1 wt% in glycolic acid) of less than about 5,000 mPas, a deacetylation degree in the range of about 80 to about 88%, and an ash content of less than about 0.3 wt%.

5. An article of manufacture according to claim 1 wherein the chitosan or chitosan derivative have an average molecular weight of about 800,000 to about 1,200,000 daltons, a Brookfield viscosity (1 wt% in glycolic acid) of less than about 5,000 mPas, a deacetylation degree in the range of about 80 to about 88%, and an ash content of less than about 0.3 wt%.

6. An article of manufacture according to claim 1 wherein the chitosan derivative is selected from the group consisting of carboxylated chitosan, succinylated chitosan and alkoxylated chitosan.

7. An article of manufacture according to claim 6 wherein the chitosan is a salt.

8. An article of manufacture according to claim 1 wherein the latex is a vulcanate and the chitosan or chitosan derivative is a vulcanization aid.

9. A protective sheath having a layer of material manufactured from latex and a coating of an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof.

10. A protective sheath according to claim 9 wherein the protective sheath is selected from the group consisting of glove, condom and bandage.

11. A protective sheath according to claim 9 wherein the chitosan or chitosan derivative have an average molecular weight of about 25,000 to about 500,000 daltons, a Brookfield viscosity (1 wt% in glycolic acid) of less than about 5,000 mPas, a deacetylation degree in the range of about 80 to about 88%, and an ash content of less than about 0.3 wt%.

12. A protective sheath according to claim 9 wherein the chitosan or chitosan derivative have an average molecular weight of about 800,000 to about 1,200,000 daltons, a Brookfield viscosity (1 wt% in glycolic acid) of less than about 5,000 mPas, a deacetylation degree in the range of about 80 to about 88%, and an ash content of less than about 0.3 wt%.

13. A protective sheath according to claim 9 wherein the chitosan derivative is selected from the group consisting of carboxylated chitosan, succinylated chitosan and alkoxylated chitosan.

14. A protective sheath according to claim 13 wherein the chitosan is a salt.

15. A protective sheath according to claim 9 wherein the coating is a gel.

16. A protective sheath according to claim 9 wherein the coating is a powder.

17. A protective sheath according to claim 9 wherein the coating is a residue resulting from evaporation of a solvent.

18. A method of reducing latex hypersensitivity reaction in an individual comprising providing an article containing latex; coating the article with an effective amount of an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof; and exposing the individual to the coated article.

19. A method of manufacturing a latex article having reduced hypersensitivity associated therewith comprising contacting and adhering the latex article with an anti-hypersensitivity agent selected from the group consisting of chitosan, chitosan derivative, anti-inflammatory agent and combinations thereof.

20. A method of manufacturing a latex article according to claim 19 wherein the latex article is prepared by dip forming over a mandrel and coating the anti-hypersensitivity agent on the mandrel prior to exposing the mandrel to latex.

21. A method of manufacturing a latex article according to claim 20 wherein the anti-hypersensitivity agent is coated in a form selected from the group consisting of gel, powder, emulsion, suspension, and solution.

22. A method of manufacturing a latex article according to claim 20 wherein the anti-hypersensitivity agent is coated on the mandrel by spraying, painting or dipping the mandrel into the anti-hypersensitivity agent.

23. A method of manufacturing a latex article according to claim 19 wherein the latex article is a glove, bandage or condom.

24. A method of manufacturing a latex article according to claim 19 wherein the anti-hypersensitivity agent is chitosan or chitosan derivative and the anti-hypersensitivity agent is contacted and adhered to the latex article by compounding the latex with the anti-hypersensitivity agent as a vulcanization aid.

25. A method of manufacturing a latex article according to claim 19 wherein the latex article is prepared by dip forming over a mandrel and coating the anti-hypersensitivity agent on the latex article after the latex article begins to congeal.

26. A method of manufacturing a latex article according to claim 20 further comprising allowing the latex article to congeal and applying a coating of an anti-hypersensitivity agent to the external surface of the latex article.

27. A method of binding water in a latex protective sheath which contacts skin comprising contacting and adhering chitosan or a chitosan derivative to a surface of the sheath which is intended to contact skin in an amount effective to bind with water.

28. A method of binding water in a latex protective sheath according to claim 27 wherein the latex prophylactic sheath is selected from the group consisting of glove, condom and bandage.

29. A method of binding water in a latex protective sheath according to claim 27 wherein the chitosan or chitosan derivative have an average molecular weight of about 25,000 to about 500,000 daltons, a Brookfield viscosity (1 wt% in glycolic acid) of less than about 5,000 mPas, a deacetylation degree in the range of about 80 to about 88%, and an ash content of less than about 0.3 wt%.

30. A method of binding water in a latex protective sheath according to claim 27 wherein the chitosan or chitosan derivative have an average molecular weight of about 800,000 to about 1,200,000 daltons, a Brookfield viscosity (1 wt% in

glycolic acid) of less than about 5,000 mPas, a deacetylation degree in the range of about 80 to about 88%, and an ash content of less than about 0.3 wt%.

31. A method of binding water in a latex protective sheath according to claim 27 wherein the chitosan derivative is selected from the group consisting of carboxylated chitosan, succinylated chitosan and alkoxylated chitosan.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/04002

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C08K5/00 C08L5/08 C08J7/04 C08L7/02 A61B19/04
A61F6/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C08K C08J A61B A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	DE 197 42 318 A (HENKEL KGAA) 1 April 1999 (1999-04-01) claims	1,2,5-8, 10,19, 24,27,31
A,P	US 5 985 955 A (BECHARA IBRAHIM ET AL) 16 November 1999 (1999-11-16) examples	1,2,9,10
A	WO 95 17453 A (CHEYMOL ANDRE ;BUSNEL RENE GUY (FR); HUTCHINSON (FR); RIESS GERARD) 29 June 1995 (1995-06-29) claims 1,10,11,19; examples	1,9,10, 17-23

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 July 2000	02/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Engel, S

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/04002

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		AT 193031 T	15-06-2000
		CA 2156267 A	29-06-1995
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		EP 0687283 A	20-12-1995
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